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## Prospective Randomised Trial of Distal Arteriovenous Fistula as an Adjunct to Femoro-infrapopliteal PTFE Bypass\*

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**Objectives:** to compare graft patency and limb salvage rate following femoro-infrapopliteal bypass using ePTFE grafts with and without the addition of adjuvant arterio-venous fistula.

**Design:** a prospectively randomised controlled trial.

**Materials:** patients referred to two teaching hospital vascular surgery units in the U.K. for the treatment of critical limb ischaemia.

**Methods:** eighty-seven patients (M:F; 2.3:1) undergoing 89 femoro-infrapopliteal bypass operations with ePTFE grafts for critical limb ischaemia were randomly allocated to have AVF included in the operative procedure ( $n=48$ ) or to a control group without AVF ( $n=41$ ). An interposition vein-cuff was incorporated at the distal anastomosis in all patients.

**Results:** the cumulative rates of primary patency and limb salvage at 1-year after operation for patients with AVF were 55.2% and 54.1% compared to 53.4% and 43.2%, respectively, for the control group. The differences between the AVF and control groups did not reach statistical significance, in terms of either graft patency or limb salvage, at any stage after operation (Log-Rank test).

**Conclusions:** AVF confers no additional significant clinical advantage over interposition vein cuff in patients having femoro-infrapopliteal bypass with ePTFE grafts for critical limb ischaemia.

**Key Words:** Randomised controlled trial; Arteriovenous fistula; Venous cuff; Patency; Prosthetic grafts.

### Introduction

High outflow resistance and low velocity of blood flow leading to thrombotic occlusion of the graft is a potential cause of early failure of femorodistal bypass surgery, especially when the indication is critical ischaemia. The alien flow surface presented by prosthetic grafts renders them more prone to this complication than grafts constructed from autologous veins and this may be a factor contributing to their comparatively poor performance. Sauvage<sup>1</sup> demonstrated experimentally that there is a characteristic velocity of blood flow for all graft materials, the thrombotic

threshold velocity (TTV), below which thrombotic occlusion is likely to occur. The purpose of an adjuvant AVF is to accelerate blood flow in the graft above the TTV level by supplementing the limited run-off provided by a severely diseased peripheral vascular bed. Although AVF has been employed, empirically, as an adjunct to femorodistal bypass surgery since the early 1980s, and improved results have been claimed,<sup>2–10</sup> its value has not previously been evaluated in a controlled trial.

One potential disadvantage of AVF is that the acceleration of blood flow, by promoting random turbulence, may aggravate problems at the distal anastomosis due to myointimal hyperplasia (MIH). Following the publication of trial results showing improved patency of ePTFE grafts with interposition vein cuffs<sup>11</sup>, and our own studies which indicate that a vein cuff modifies, beneficially, anastomotic MIH, it has been our practice to apply it at the distal anastomosis

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**Table 1.** Clinical characteristic of patients in AVF and control groups

	AVF	Control
Age (mean)	71.5	69.1
Sex M:F	1.4:1	4.8:1
Indication	Rest pain established necrosis	Rest pain established necrosis
Smoking	72.5%	64.4%
Diabetes	17.5%	15.7%
Outflow vessel:		
Anterior tibial	35%	29%
Peroneal	35%	34%
Posterior tibial	30%	37%

of all prosthetic femoro-infrapopliteal bypasses. Therefore, the aim of the trial reported here was to determine whether AVF provided any additional clinical advantage over interposition vein-cuff in patients having femoro-infrapopliteal bypass surgery for critical limb ischaemia.

## Patients and Methods

### Patients

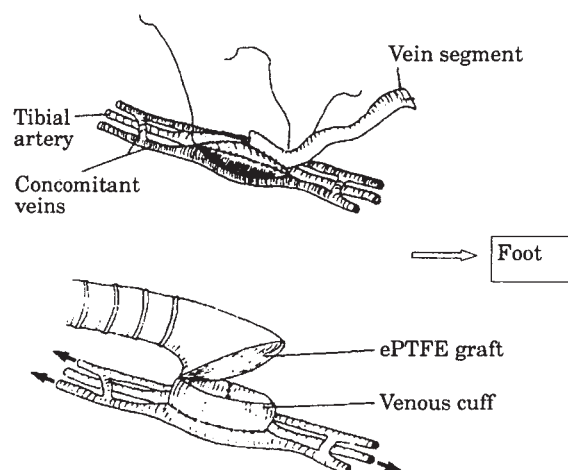
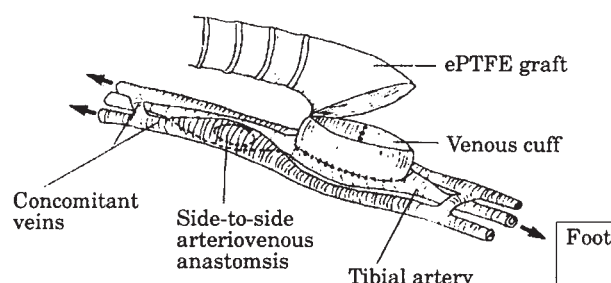
The vascular surgical services of two U.K. teaching hospitals, Royal Liverpool University Hospital, Liverpool and Chelsea and Westminster Hospital, London, participated in this trial.

A total of 89 femoro-infrapopliteal bypasses using ePTFE grafts, carried out in 87 patients with critical limb ischaemia, were included between June 1991 and June 1997. The mean age of the patients was 70.3 years (range 31–89 years) and the male to female ratio was 3.2:1. Fourteen were diabetic and 57 admitted to smoking within the last year. All had critical limb ischaemia as defined by the European Consensus Document.<sup>12</sup>

Forty-eight were randomly allocated to receive an adjuvant AVF and 41 to a control group. Clinical characteristics of the patients in each group are shown in Table 1. Local ethical committee approval was obtained prior to the commencement of the trial. Patients, who consented to take part, were recruited consecutively. Exclusion criteria were: (i) the presence of autologous vein suitable for vein graft; (ii) venous hypertension due to deep venous obstruction in the affected limb; (iii) severely compromised cardiac function.

### Surgical technique

Patients were operated upon under general anaesthesia and received antibiotic prophylaxis in the

**Fig 1.** Common ostium fistula.<sup>16</sup>**Fig 2.** Pre-anastomotic fistula.<sup>16</sup>

form of Cefotaxime 1.5 gm intravenously at induction. Externally supported 6 mm ePTFE grafts (Impra Corp) were employed in all cases. The distal anastomosis was constructed in end-to-side manner with an interposition vein-cuff.<sup>13,14</sup>

A common ostium fistula (Fig. 1) was constructed in patients in whom the concomitant veins related to the recipient artery were judged to be small, and a pre-anastomotic fistula (Fig. 2) was used in those with larger concomitant veins. In all cases the use of clamps was avoided, prevention of back bleeding being achieved with fine intraluminal silicone catheters. Antiplatelet therapy in the form of aspirin 300 mg daily was commenced at least 48 h preoperatively. All patients received heparin 5000 iu during operation and anticoagulation was continued for 5 days after operation with a continuous infusion of heparin, the dose of which was adjusted to maintain APPT levels within a therapeutic range of 2–3 times normal value. All patients were discharged on oral warfarin in addition to the aspirin which had been commenced preoperatively, this anticoagulation regime being continued indefinitely.

Follow-up was by clinical examination and duplex ultrasound scanning in the vascular laboratory at 6 weeks, 3, 6, 9 and 12 months after operation and then

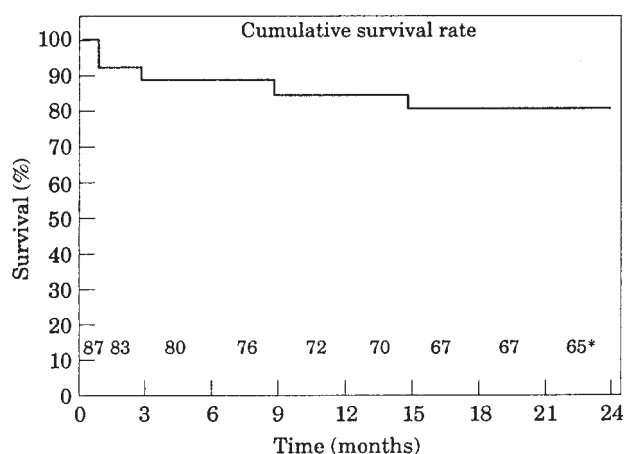


Fig. 3. Cumulative survival rate of all patients. adjusted number aof patients at risk.

at variable intervals thereafter. All patients in whom graft occlusion was suspected were investigated further by angiography.

The results, in terms of graft patency and limb salvage, were analysed by calculation of Kaplan-Meier curves,<sup>15</sup> and Log-Rank test was applied to test for statistical significance.

## Results

Five patients died within 30 days of operation, giving a perioperative mortality rate of 5.6%. The cumulative survival rate of all patients at 6, 12, and 24 months was 91%, 85.3% and 81.6%, respectively (Fig. 3).

The construction of an adjuvant AVF increased the operating time by an average of approximately 30 min.

In the AVF group five grafts occluded within the first month after operation and this was followed by early loss of the limb in four. Another 15 grafts became occluded within the first year, only one of which was re-explored with restoration of patency. This graft became occluded again within 14 h.

In the control group 10 grafts occluded within the first month and this was followed by early amputation in seven. One patient underwent thrombolysis and re-exploration with the elective addition of an AVF that restored graft patency for another 6 months. Another 14 grafts in the control group occluded within the first year, two of which were re-explored and one treated by thrombolysis followed by angioplasty of the inflow vessel (Tables 5, 6). A worthwhile period of patency was restored in only one of these patients.

The primary and secondary cumulative patency rates and the cumulative limb salvage rate for patients

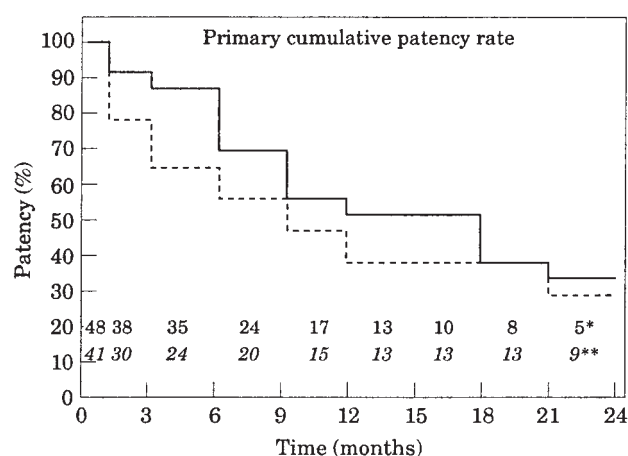


Fig. 4. Primary cumulative patency rates of the AVF group in continuous line (—) and the control group in dashed line (.....).

\* Adjusted number of patients at risk of the AVF group

\*\* Adjusted number of patients at risk of the control group

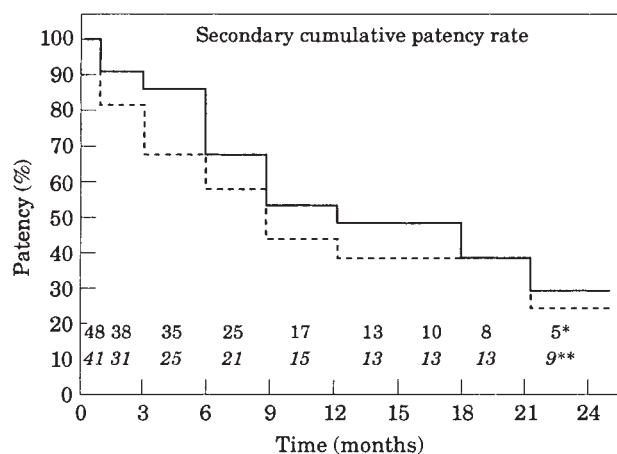


Fig. 5. Secondary cumulative patency rates of the AVF group in continuous line (—) and the control group in dashed lines (.....).

\* Adjusted number of patients at risk of the AVF group

\*\* Adjusted number of patients at risk of the control group

with AVF and controls are shown in Figs 4, 5 and 6. There was no statistically significant difference between the two groups with respect to primary and secondary patency rate ( $p > 0.2$  Log-Rank test) or limb salvage rate ( $p < 0.3$  Log-Rank test) at any stage after operation. A trend towards better early patency of grafts with adjuvant AVF diminished progressively after the first 6 months.

## Discussion

A previously reported study from Liverpool<sup>16</sup> indicated that, although interposition vein-cuff (VC) did improve the patency rate of long, distal ePTFE grafts in keeping with the findings of the JVRG (Joint Vascular

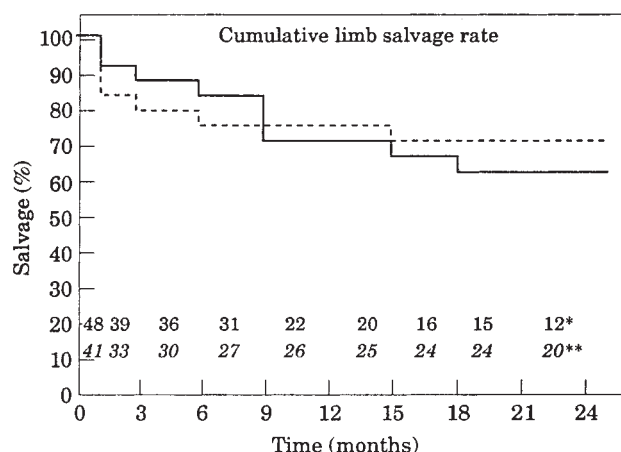


Fig. 6. Cumulative limb salvage of the AVF group in continuous line (—) and the control group in dashed line (.....).

\* Adjusted number of patients at risk of the AVF group

\*\* Adjusted number of patients at risk of the control group

Research Group) trial,<sup>11</sup> the effect of AVF was rather more dubious. A prospectively randomised controlled trial was required to establish whether or not AVF has any clinical value.

The reported results of autologous vein grafts for femoro-infrapopliteal bypass are considerably superior to those of prosthetic grafts including ePTFE.<sup>17</sup> Therefore, autologous vein is used in preference to ePTFE whenever possible, and this accounts for the fact that two large vascular surgery units were able to recruit into this trial only 87 patients in 6 years. The relatively small number of patients undermines the power of the trial and it is possible that a significant early advantage for AVF, in terms of primary patency, may have been masked by a type two statistical error. However, the observed early trend in favour of AVF diminished progressively after the first 6 months. The rates of limb salvage in AVF and control groups were very closely matched at all stages after operation. Therefore it is probably safe to conclude from the results of this trial that AVF confers no durable clinical benefit.

It would be interesting to know what proportion of adjuvant A-V fistulae remained patent and whether closure of the fistula increased the risk of graft failure. Graft thrombosis was always accompanied by closure of the fistula, and it was not possible to determine which occurred first in these circumstances. A small number of grafts have remained patent despite closure of the AVF, but the great majority of patent grafts in the AVF group also had a patent AVF. The absence of precise information in this respect does not undermine the principle conclusion that can be drawn from the trial.

Venous hypertension and steal phenomena are often

cited as potential complications of adjuvant AVF. In this trial deep veins only were used for the construction of the AVF and patients with a known history of deep vein thrombosis in the relevant limb were excluded. Only two patients developed evidence of clinically significant venous hypertension. It is known that a steal of blood from the foot is likely to occur only if inflow to the graft is impeded<sup>18</sup> and care was taken to ensure that this situation was avoided. Although one patient in the AVF group required amputation despite a patent graft, this was attributable to a large volume of irreversible ischaemia within the foot. No clinical consequences due to steal phenomena were recognised in any of the patients.

Extremely low patency rates, of 30% or less, reported from the use of ePTFE grafts for femoro-infrapopliteal bypass have fuelled the controversy concerning the relative merits of reconstruction and primary amputation in the absence of autologous vein. However, cumulative patency rates in excess of 50% after the first year for ePTFE grafts with interposition vein cuff, as reported by the Joint Vascular Research Group of Great Britain and Ireland<sup>11</sup> and again here, suggest that reconstruction is certainly the best option for the majority of patients. However, the results of this trial indicate that the addition of AVF confers no worthwhile advantage above that which can be achieved with interposition vein cuff alone. Therefore, the application of adjuvant AVF as routine is not justified.

Many surgeons can report anecdotal experience of having secured worthwhile patency of a graft following early secondary intervention that included the construction of an AVF. One graft in the present series remained patent for 6 months under these circumstances. In this context the following points are worth making; first, harmful effects attributable to AVF are rare, and second, the results of this trial cannot be taken to exclude the possibility that individual patients may occasionally benefit from the application of AVF under exceptional circumstances.

In summary, the results of this prospectively randomised trial do not show evidence of worthwhile benefit associated with AVF, in terms of either graft patency or limb salvage rates, and it is concluded, therefore, that there is no indication for its routine application with prosthetic femoro-infrapopliteal bypass grafts.

## References

- 1 SAUVAGE LR, WALTER MW, BERGER K *et al.* Current arterial prostheses. Experimental evaluation by implantation in the carotid and circumflex coronary artery of the dog. *Arch Surg* 1979; 114: 687-691.

- 2 DARDIK H, BERRY S, DARDIK A *et al.* Infrapopliteal prosthetic graft patency by use of the distal adjunctive arteriovenous fistula. *J Vasc Surg* 1991; **13**: 685–691.
- 3 DAVIS P, HENEGONWEN B, STELZER G *et al.* Pedal and distal lower leg bypasses with a distal arteriovenous fistula. *Eur J Vasc Surg* 1987; **1**: 251–258.
- 4 JACOBS M, REUL G, GREGORIC I *et al.* Creation of a distal arteriovenous fistula improves microcirculatory hemodynamics of prosthetic graft bypass in secondary limb salvage procedures. *J Vasc Surg* 1993; **18**: 1–9.
- 5 IBRAHIM I, SUSMAN B, DARDIK I *et al.* Adjunctive arteriovenous fistula with tibial and peroneal reconstruction for limb salvage. *Am J Surg* 1980; **140**: 246–251.
- 6 CHARLESWORTH PM, BREWSTER DA, DARLING RC *et al.* The fate of polytetrafluoroethylene grafts in lower limb bypass surgery: 6-year follow-up. *Br J Surg* 1985; **72**: 896–899.
- 7 PARSONS R, SUGGS W, VEITH F *et al.* Polytetrafluoroethylene bypasses to infrapopliteal arteries without cuff or patches: a better option than amputation in patients without autologous vein. *J Vasc Surg* 1996; **23**: 347–356.
- 8 KORTMANN H, OREND KH, ABENDROTH D, BECKER HM. Crural arterial reconstruction with adjuvant arteriovenous fistula for limb salvage. *Thorac Cardiovasc Surgeon* 1985; **33**: 382–384.
- 9 ASCER E, GENNARO M, POLLINA RM *et al.* Complementary distal arteriovenous fistula and deep vein interposition: a 5-year experience with a new technique to improve infrapopliteal prosthetic bypass patency. *J Vasc Surg* 1996; **24**: 134–143.
- 10 DARDIK H, SILVESTRI F, ALASIO T *et al.* Improved method to create the common ostium variant of the distal arteriovenous fistula for enhancing crural prosthetic graft patency. *J Vasc Surg* 1996; **24**: 240–248.
- 11 STONEBRIDGE PA, PRESCOTT RJ, RUCKLEY CV. Randomised trial comparing infra-inguinal polytetrafluoroethylene bypass grafting with and without vein interposition cuff at the distal anastomosis. The Joint Vascular Research Group. *J Vasc Surg* 1997; **26**: 543–550.
- 12 EUROPEAN WORKING GROUP ON CRITICAL LEG ISCHAEMIA. Second European Consensus Document on chronic critical leg ischaemia. *Circulation* 1991; **84** (Suppl. 4): 1–26.
- 13 MILLER JH, FORMANN RK, FERGUSON L, FARIS I. Interposition vein-cuff for anastomosis of prosthesis to small artery. *Aust NZ J Surg* 1984; **54**: 283–285.
- 14 HARRIS PL. Adjuvant arteriovenous fistula at the distal anastomosis of a femorotibial bypass graft. In: Greenhalgh RM, ed. *Vascular Surgical Technique: An Atlas*. London, England: WB Saunders, 1989; 306–309.
- 15 UNDERWOOD CJ, FARAGHER EB, CHARLESWORTH D. The uses and abuses of life table analysis in vascular surgery. *Br J Surg* 1984; **71**: 495–498.
- 16 HARRIS PL, BAKRAN A, ENABI L *et al.* ePTFE Grafts for Femorocrural bypass-improved results with combined adjuvant venous cuff and arteriovenous fistula? *Eur J Vasc Surg* 1993; **7**: 528–533.
- 17 VEITH FJ, GUPTA SK, ASCER E *et al.* Six-year prospective multicentre randomised comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. *J Vasc Surg* 1986; **3**: 104–114.
- 18 CAMPBELL H, HOW TV, HARRIS PL. Experimental evaluation of arterial steal in *in vitro* models of femoro-tibial bypass with adjuvant A–V shunt. *Clin Phys Physiol Measurement* 1984; **5**: 253–262.

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